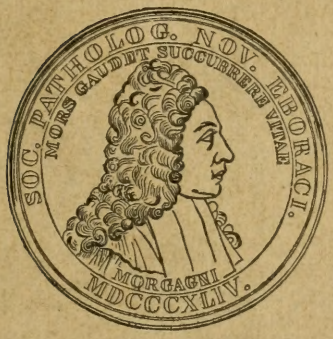
RB
1
V32
2 S.
V. 11
no. 5/6
Biological
& Medical
Serials

New Series, Vol. XI. Nos. 5 and 6

PROCEEDINGS

OF THE

NEW YORK PATHOLOGICAL SOCIETY



LIBRARY
UNIVERSITY OF TORONTO
Exchange

November and December, 1911

PUBLISHED BY THE SOCIETY

ALWIN M. PAPPENHEIMER, Editor
Pathological Laboratory, Bellevue Hospital, New York, N. Y.

Proceedings

of the

New York Pathological Society.

New Series, Vol. XI. NOVEMBER AND DECEMBER, 1911 Nos. 5 and 6

TABLE OF CONTENTS.

KIRKBRIDE, The Islands of Langerhans After Ligation of the Pancreatic Duct.—MACCALLUM, Carcinoma of the Stomach, With Curious Metastases in the Lungs.—RUBIN, A Case of Ovarian Pregnancy.—PAPPENHEIMER, Demonstration of a Case of Hemochromatosis.—MOSCHOWITZ, Carcinomatous Infiltration of the Solar Plexus.—EWING, A Case of Mesenteric Thrombosis.—NORRIS, A Large Tumor of the Liver Associated With a Tumor of the Oesophagus.—BAEHR, Specimens from a Case of Bismuth Poisoning.—LIBMAN, Demonstration of the Cardiac Lesions of Subacute Bacterial Endocarditis.—BAEHR, Glomerular Lesions of Subacute Bacterial Endocarditis.—COHN, Demonstration of Specimens, Illustrating a New Method of Injecting the Conduction System of the Heart.—GERSTER, Gigantism Affecting the Bones Only, Complicated by Traumatic Ostoses.

DR. W. G. MACCALLUM, *President.*

THE ISLANDS OF LANGERHANS AFTER LIGATION OF THE PANCREATIC DUCTS.

MARY BUTLER KIRKBRIDE, M.D.

The question of the persistence of the islands of Langerhans after ligation of the pancreatic ducts is of special importance when regarded from the standpoint of the relation of the islands to glycosuria. While it has been shown that glycosuria invariably occurs after complete removal of the pancreas, it has generally been accepted that ligation of the pancreatic ducts is not followed by glycosuria.

In 1909, MacCallum described an experiment in which one-third of the pancreas of a dog was separted from the main mass and the ducts ligated. Seven months later when this isolated portion was reduced to a mere thickening of the mesentery, the normal remainder of the gland was removed. Glycosuria followed but was slight, and lasted only three days, after which time a very considerable tolerance for sugar was attained. When, twenty-one days later, the pancreatic remnant was removed, extreme glycosuria resulted. Microscopically, this remnant showed masses of cells which, though morphologically like islet cells, were not so typical as to eliminate all doubt in this respect.

The present study was undertaken for the purpose of ascertaining by means of differential stains whether these groups of cells described by MacCallum and others were made up solely of persisting islet tissue By means of Lane's method the desired contrast in the staining reaction between the acinar and the islet cells was obtained. The pancreas taken from a normal guinea pig showed the islet cells filled exclusively with fine dark blue granules, while the zymogen granules of the acinar cells stained a reddish brown. The isolated pancreatic portion of a guinea pig, which had been operated on three weeks before, showed an increase of connective tissue, and the acinar cells greatly shrunken, while the islands of Langerhans appeared normal and their cells filled with blue granules. A third guinea pig was operated on in the same way and kept for nearly fifteen months. Microscopic examination of the fatty mass, which had replaced the isolated portion of the pancreas, showed no trace of acinar cells. But embedded in it were found small groups of cells whose cytoplasm was filled with typical blue granules. There could be no doubt that these cells belonged to persisting and actively functioning islands of Langerhans.

Several points are suggested by this preliminary study. First, that the contrast in the staining reaction between the granules of the acinar and the islet cells, as shown by Lane, can be confirmed. Secondly, that during the atrophy of the acinar cells and even long after the last traces of them have disappeared, the

islet cells remained morphologically unaffected and filled with the granules which are peculiar to them. Taken together with the experiments of Dr. MacCallum, this seems to offer strong evidence in support of the view that the islands of Langerhans are especially, if not exclusively, concerned with the maintenance of the normal carbohydrate metabolism.

Discussion.

Dr. Ewing: I would like to ask if in the course of changes observed in these tissues, there was any evidence encountered of transformation of ordinary acinar cells into the type of islet cells?

Miss Kirkbride: In some sections, I have occasionally found places where it is very difficult to say positively whether one has, or has not, to do with transitional forms. But, on the whole, I am inclined to think there are no transitions between the acinar and the islet cells.

CARCINOMA OF THE STOMACH WITH CURIOUS METASTASES IN THE LUNGS.

W. G. MAC CALLUM, M.D.

The peculiar lesions which appeared in the lungs in this case seemed to justify its being reported. The specimens were taken from a man aged 55 years who died with obscure symptoms of the growth of a malignant tumor in his lung. Nevertheless at autopsy the appearances were, at first sight, those of tuberculous infection of the lung. There were areas of consolidation scattered about through both lungs which on section had almost exactly the appearance of a pneumonic consolidation while the remaining lung tissue was studded here and there with small tubercle-like masses. There were, however, small lenticular thickenings of the pleura which suggested rather a tumor growth.

Examination of the abdominal viscera revealed a tumor of the stomach which occupied a large portion of the pyloric end of the stomach. It produced a diffuse thickening of the wall, but there was practically no ulceration and no marked contraction. The glands in the neighborhood of the pylorus and the head of the pancreas were involved, and the pancreas itself was somewhat invaded. The discovery of these lesions made fairly certain the diagnosis of secondary cancerous involvement of the lung.

The point of especial interest is the microscopical character of the growth in the lungs. The tumor, which had grown largely in the lymphatic channels, the walls of the arteries and veins, frequently leaves them and enters the alveoli, and in the areas which appeared to be consolidated, every alveolus is snugly filled with a mass of tumor cells. In none of these alveolar masses of cells could any blood vessels be found, and it seems as though the cells were growing there, bathed in the fluid which fills most of the alveoli and produces the condition of oedema throughout a large part of the lung. In this respect their growth resembles very closely that which one sees in the cultures of carcinoma cells made in a hanging drop of plasma on a slide.

The epithelial cells hang together very closely, as has been pointed out by Drs. Lambert and Hanes, in these cultures when the tissue employed is from a carcinoma; and are in sharp contrast in this respect with the cells of a sarcoma which tend to separate from one another and grow out independently. So, too, in the alveoli of the lung, the epithelial cells grow in solid masses with fairly smooth outlines, and one can hardly escape the impression that they find there a suitable nutritive medium and mechanical support and in which they grow practically as they would in vitro.

Discussion.

Dr. Norris: You see occasionally the microscopic picture which Dr. MacCallum has shown in the slides, when there occurs an aspiration of cells. Thus, when rupture occurs of softened epitheliomatous lymph-nodes into a bronchus, aspiration into the lobules takes place, and produces a similar appearance.

A CASE OF OVARIAN PREGNANCY.

I. C. RUBIN, M.D.

The patient from whom I removed this specimen was 24 years old, had been married three years, had one child two years of age. Previous and family history are of no interest in this case. Last menstrual period seven weeks before admission to hospital, which was a year ago last July. Patient was admitted to Beth Israel Hospital, in the service of Dr. S. W. Bandler. Two months before admission to hospital, she had rather sharp pain in the abdomen, localized especially in the lower half and more intense on the right side than on the left. At that time she noted a yellowish vaginal discharge; she had pains once or twice daily during the two months previous to admission; she also reported feeling chilly and feverish at times. Two days before admission there was vaginal bleeding. At the time of admission we noticed no bleeding of any kind, either at the vulva or escaping from the external os. Examination vaginally, elicited tenderness on the left side over a mass which seemed to be twice as large as an average normal ovary, but did not have the characteristic hardness. The ovary on the right side was also enlarged and tender.

The diagnosis made, in view of the irregular history, was ectopic gestation on the left side, also possibly associated with inflammatory disease. Gonococci were not found in either the vaginal or urethral smears.

On opening the abdomen, my attention was directed to a small amount (about 2 ounces) of yellowish fluid which was bloody, and which seemed to fill the posterior cul-de-sac. The uterus was in good position, though somewhat enlarged. The left adnexa were enlarged. The tube was bent backward. The ovary was attached to the posterior aspect of the broad ligament close to the uterus. On trying to deliver the ovary, I noticed that in the area of attachment to the posterior ligament there was a rather irregular, chocolate-brown mass which protruded from the ovary, and which looked very much like a degenerated corpus luteum. At the same time, in the manipulation, I brought to

view a small plum-colored mass, about the size of a hazel nut. I was not certain at the time whether it was a corpus luteum or a bloody mole. The uterine serosa seemed oedematous and tore through when grasped with tenaculum or forceps.

The tube was removed at its uterine insertion. The right adnexa showed cystic degeneration of the ovary. The tubes on either side were practically normal. One point of interest was that the left tube was rather short. I did not notice whether it was short in comparison to the right, but after straightening it out, I saw it was a short tube.

Patient made an uneventful recovery. I curretted her without anaesthesia, after waiting two weeks for the possible discharge of a decidual cast, and examined the currettings as well to make the study of the case complete. The specimens that I examined were the left adnexa, a small portion of the ovary of the right side and the uterine currettings. Under the microscope one of these sections showed a blood clot surrounded practically on all sides by an ovarian cortex. The first section taken through the apparent level of the rupture showed very few chorionic villi; these were in a very poor state of preservation. There was not the typical double layer of epithelium but the myxomatous stroma was so characteristic that there was no question about it. Another section showed groups of these chorionic villi, unquestionable in character, which were immediately underlying the ovarian cortex. The cortex itself showed a comparatively normal structure. There were typical ovarian elements, *i. e.*, follicles in all stages of development, from the earlier form to the mature follicle. On the surface of one portion of the ovary were several groups, spherical and ovoid, which showed characteristic decidual cells. These were separated by a cleft which was lined by flat cells that resembled endothelial cells but on comparison with some of the residual germinal epithelium, I am inclined to think they are true epithelial cells. There was no remnant of the corpus luteum except for a number of pigmented cells at the circumference of the blood coagulum, some of which suggested very strongly typical luteal cells. The tube on the same side, several sections being

made, showed no decidual reaction whatever. The ovary of the other side—the small piece that was examined—showed a rather peculiar condition of what might be called a theca-lutein cyst. I mention that to submit it for your consideration, as I am not quite certain about its significance. The uterine currettings showed nothing striking. I was surprised not to find any evidence of decidual reaction.

Another point which is of some interest in this specimen is the appearance of decidual cells within the walls of the smallest blood vessels within the ovarian cortex in the close vicinity of the decidual tubercles mentioned above. Most of the microscopic sections show this change within the vessel walls, though the decidual tubercles appeared in sections of a small portion of the ovary.

Since grossly the ovary was the seat of a pregnancy, since the tube on the same side did not show any fetal elements, and since, further, the ovary was undoubtedly connected to the uterus by the utero-ovarian ligament, and lastly, since the chorionic elements were found microscopically in the blood clot, immediately surrounded on all sides by ovarian cortex, the diagnosis of ovarian pregnancy seems absolutely certain, and satisfies all the criteria laid down by Spiegelberg, Williams, Norris, and others.

The ovary measured about 6.5 x 4.5 x 2.5 cm.

Discussion.

Dr. Norris asked Dr. Rubin whether any serial sections were made of the ovary.

Dr. MacCallum: The most interesting point in this connection is the behavior of the corpus luteum. In a case seen last year in which the ovarian pregnacy was very definitely determined, the formation of lutein tissue was quite striking throughout both ovaries, and it seemed possible that since the follicle in which pregnancy was going on could scarcely carry on a normal formation of corpus luteum, similar tissue was formed in an unusual degree in other parts of the ovaries.

Dr. Rubin said that he did not make serial sections but cut out sections of various parts of the ovary. He preserved the ovary so that it could be demonstrated at future times.

DEMONSTRATION OF A CASE OF HEMOCHROMATOSIS.

A. M. PAPPENHEIMER, M.D.

The case is one from Dr. Janeway's service, and I am indebted to him for permission to report the clinical data. The essentials of the history are as follows: Man 37 years of age, alcoholic, had taken ten or twelve whiskeys a day. He became ill in March, developing symptoms of an acute diabetes with 4 to 7 per cent. of sugar in his urine. The liver was enlarged. There was rapid loss of weight, acidosis developed and the case terminated with high fever and symptoms of general infection. There was not noted, during the time the case was observed clinically, any striking pigmentation of the skin, but at the autopsy the skin is described as having a slight leaden hue and there were noted some patches of pigmentation, resembling freckles, on the surface of both forearms.

The autopsy was performed by Dr. Hanes, from whose protocol I abstract the following notes: On opening the abdominal cavity there is found an excessive amount of free fluid of dark-yellow color, and rather turbid. Adhesions about upper lobe of spleen and left lobe of liver. Heart and lungs practically normal. Spleen greatly enlarged, weight 570 gms., measuring 16 x 11 x 5½ cm., firm; there was a thick yellow deposit on the capsule. On section it was smooth, with no bulging of the pulp. There was no marked change in the color. The liver was large, weighed 2580 gms. The color of the liver was exceedingly striking; both on the surface and on section it presented a very typical, chocolate or bronze color characteristic of the affection. It showed a fine diffuse cirrhosis and a number of whitish foci, some with central softening, which proved to be abscesses or areas of necrosis. The stomach mucosa was considerably congested; it showed no striking pigmentation, although the mucosa was very thick and velvety. The rest of the intestinal tract showed nothing remarkable. Kidneys negative. Bladder negative. Perigastric and retro-peritoneal lymph-nodes and the pan-

creas showed the most extreme macroscopic changes, the cut sections presenting the typical chocolate or mahogany brown appearance. The pancreas was very firm, but neither enlarged nor atrophic.

Microscopic Examination.

Skin: One of the small pigmented spots on the chest was taken for examination. The Malpighian layer of the epidermis is free from pigment, but there is an abundant deposit of yellow granules giving the iron reaction, about the basement membranes of the sweat glands. The glandular and duct epithelium itself is free. This is a rather striking exception to the general rule that the pigment is deposited primarily in the glandular epithelium.

Liver: The liver lobules, which are of large size and irregular shape, are separated by stout fibrous septa, in which are many new-formed bile ducts. The liver cells stain well, and for the most part show no degenerative changes. They contain, without exception, masses of yellowish pigment granules giving the "hemosiderin" reaction, and showing a characteristic distribution in the distal supra-nuclear portion of the cells—away from the blood capillaries. The nuclei themselves are invariably free from blood pigment. In the interlobular connective tissue, the pigment lies in part within the connective tissue cells, in part scattered between the hyaline fibrils. The endothelial cells of the capillaries and of the larger vessels as well, contain it, as do the epithelial cells of the new-formed bile-ducts. The larger bile-ducts are relatively free.

The large abscesses are composed of necrotic material with much chromatin dust, pycnotic material and, at the periphery, a loose granulation tissue in which are numerous lymphoid and plasma cells. There is considerable iron-reacting intra and extracellular pigment scattered through the necrotic areas, and in places, the persitent liver framework is encrusted with iron salts, staining also with hematoxylon. To this peculiar incrustation, we shall refer again.

Pancreas: In this organ, also, there is a very pronounced sclerosis, which is both inter and intra-lobular in type. The pigment is extremely abundant, both within the parenchymal cells and in the stroma. Here, as in the liver, there is a distinct tendency for the pigment to be massed in the inner portion of the acinal cells, surrounding the lumen. The larger pancreatic ducts contain little or no pigment.

Very few islands of Langerhans were found in the sections examined. None of those discovered show marked fibrosis or hyalin change. Some of the island cells contain a good deal of coarse pigment, others are entirely free. On the whole, the islands contain decidedly less pigment than the acinal portions of the gland.

Adrenal: Here the pigment is virtually limited to the extreme outer portion of the zona glomerulosa, rarely extending a short distance into the fasciculate zone. The capsule is entirely free, and the pigment granules are apparently situated within the parenchymal cells, and not in the stroma. A few scattered pigment-bearing cells are found also in the medullary portion of the gland about the central vein—whether within chromaffin cells or not, it is difficult to say.

Spleen: Is congested. In the sinuses are many large endothelial (?) cells, with stippled protoplasm and small, deeply staining, eccentric nuclei. Many of these cells contain a few greenish-yellow pigment granules of small size.

The Malpighian bodies are small; the central artery is slightly sclerosed.

The trabeculae are not much thickened, but in many of them are irregular fibers staining bluish with hematoxylin, but giving a pronounced iron reaction with Perl's method. Under the immersion, the elastic fibers may be traced directly into these blue-staining fibers; one gets the impression, however, that the blue-staining material is deposited upon or along the refractile fibers, and one may occasionally follow an elastic fiber as a refractile central core, directly through the bluish portions. Some of the small blood-vessels are also wholly or incompletely con-

verted into thick, rigid, blue-staining rings. The incrustation involves practically the entire muscular coat as well as the elastic fibers.

Lymph-nodes: Corresponding to the gross appearance, there is an enormous deposition of pigment in the mesenteric and peri-pancreatic lymph-nodes. In contrasting sections stained according to Perl's methods with those treated after Nishimura, with ammonium sulphide, followed by potassium ferrocyanide and HCl, one finds that the latter show an even greater amount of iron reacting pigment. The granules occur intra-cellularly, particularly in the endothelial cells of the lymph-sinuses, in giant-cells, and in free clumps between the cellular elements. There is a fairly marked fibrosis of the glands.

A very remarkable feature is the conversion of the reticulum in places into a dense, rigid framework which in part appears as a greenish refractile substance, in part stains a deep blue with hematoxylin. In places, these incrusted fibers have fragmented into short, thick bars, many of which are surrounded by large, foreign body giant cells, containing a dozen or more nuclei.

With the iron stains, the incrusted reticulum yields an intense blue color. Treated with a silver nitrate solution, a part at least of the reticulum stains black after exposure, demonstrating the presence of phosphates. Although the avidity of these structures for the hematoxylin as well as their refractile appearance in unstained sections, strongly suggested the presence of calcification, it was found that after treatment with a strong oxalic acid solution, they no longer stained with aqueous hematoxylin. This applies also to the incrustation of the walls of the small arteries, which showed the same lesion as those in the spleen.

One further feature is worth recording, namely, the occasional presence within the giant-cells of peculiar stellate inclusions, similar to those described and pictured by Wolbach (*J. of Med. Res.* Vol. XXIV., No. 2, 1911) and more recently by Vogel in a case of Bronchiolitis obliterans (*Virch. Arch.* Bd.

206, Hft. 1, 1911). These inclusions do not give the iron reaction, nor stain directly with the orcein elastic tissue stain.

Myocardium: The pigment is abundant. It shows a tendency to be massed about the poles of the nuclei in the undifferentiated sarcoplasma, but rows of granules extend also a considerable distance between the fibrillae. The interstitium is practically free from pigment.

Stomach: In the gastric mucosa, there is a fairly abundant deposit of pigment in the depths of the glands. The more superficial layer of the epithelium as well as the muscularis, is quite free. One observes again the tendency of the pigment to accumulate in that portion of the secreting cell which is next to the lumen of the gland tubule and away from the basement membrane. This is very distinct in cross sections, where the lumen is seen lined with blue granules.

From the above report, it is evident that the case is a very typical one, resembling closely, both in the clinical and pathological features, many of the previously observed cases. The conflicting and inadequate theories regarding the pathogenesis of the disease, have been excellently summarized by Sprunt in a recent article (*Arch. of Int. Med.*, Vol. 8, No. 1, 1911), and need not be discussed here. The features of particular interest in this case are, perhaps, the absence of noteworthy changes in the islands of Langerhans, in spite of the intense glycosuria, and the remarkable iron incrustation of the elastic and reticular fibers of the lymphnodes and splenic trabeculae.

(Sections of the organs above described were demonstrated with the projection apparatus.)

Discussion.

DR. EWING: In a case of hemochromatosis examined by Dr. Elser, of the New York Hospital, some years ago, and used in our laboratory for class demonstration, the pancreas differed essentially from that described by Dr. Pappenheimer, in that it

showed an enormous increase in the number and size of the islands. These occupied in some places at least half of the parenchyma.

Dr. Libman: About six or seven years ago we had a very interesting case of diabetes in which at post-mortem examination we found marked hemosiderosis of the liver and spleen, but none of the pancreas. There was present a hyaline degeneration of the islands of Langerhans. We considered this case of some importance because it demonstrated that the explanation given by certain authors of the pathogenesis of bronzed diabetes cannot hold in all instances. According to these authors, there is first a hemosiderosis of the pancreas, and later a cirrhosis of the pancreas, this leading to a glycosuria. In the case which I have mentioned, this could not hold true.

CARCINOMATOUS INFILTRATION OF THE SOLAR PLEXUS.

ELY MOSCHCOWITZ, M.D.

J. S., 48 years old. The esential facts in his clinical history are these: Gradually increasing jaundice of fourteen months duration accompanied by a gradual loss of weight. For the past four weeks, attacks of pain in the abdomen, which were relieved by catharsis. Physical examination, with the exception of a deep jaundice, was negative. At exploratory operation, the pancreas was found enlarged; a few small nodules on the upper surface of the liver were noted, one of which was removed and from a frozen section was reported adeno-carcinoma. A cholecystectomy was done. The patient died 24 hours later.

The autopsy was incomplete. A firm mass was found lying above the pancreas and surrounding the superior mesenteric artery. The mass was irregular in outline, densely adherent to the pancreas, firm and grey. Superiorly it merged gradually into

the surrounding retro-peritoneal tissues. On section, small cone-shaped projections are distinctly visible upon pressure, which recede as the pressure is released. Numerous smaller and larger bile-stained glands are present, within and surrounding this mass.

The primary tumor was apparently not removed at autopsy, but was probably situated either in the terminal portion of the biliary passages or in the duodenum. The condition of the remaining organs at autopsy is indicated by the *Anatomical Diagnosis:* Obstructive Jaundice. Metastatic Carcinoma of the liver and pancreas. *Interstitial pancreatitis.* Dilatation of the gall-bladder: fresh cholecystectomy; Periportal cirrhosis with fatty degeneration and bile pigmentation of the liver. Hyperplasia and chronic congestion of the spleen. Fatty and parenchymatous degeneration of the kidneys.

Microscopical Examination.

The nodules of the *liver* showed typical adeno-carcinoma. The organ otherwise shows chronic congestion and slight periportal cirrhosis.

Spleen: Chronic congestion. *Kidneys:* Chronic diffuse nephritis. *Pylorus and portion of duodenum removed:* Negative. *Pancreas:* There is a marked cirrhosis with an abundant increase in the peri-acinar and interlobular connective tissue. There is much round-celled infiltration. The acini are distorted in shape, due to the growth of the peri-acinar connective tissue. Numerous islets of adeno-carcinoma are present in the interlobular connective tissue, especially in the head of the pancreas. The connective tissue around the biliary passages shows a number of islets of adeno-carcinoma. The nerves in this situation show infiltration with adeno-carcinoma similar to that about to be described.

The mass lying above the pancreas consists of numerous nerve bundles and connective tissue, fat, areolar tissue and lymphatic glands. It is apparent from the relations of this mass to

the pancreas and the superior mesenteric artery that the collection of nerve bundles constitutes in the main the superior mesenteric or solar plexus.

Only a small minority of the nerve bundles have escaped carcinomatous invasion.

The majority of the nerves show a carcinomatous infiltration, which is distributed in three ways.

1. The carcinoma is strictly limited to the perineurium. (Fig. 1).

2. The carcinoma is strictly limited to the endoneurium. (Fig. 2).

3. Both perineurium and endoneurium are involved. (Fig. 3).

In many instances, there is evidence of continuity between the perineural and endoneural carcinomatous acini, and between the perineural invasions and small infiltrations lying just outside the perineurium. The epineurium otherwise is remarkably free from carcinomatous invasion.

The nerve bundles are very large and show areas of degeneration, more or less complete.

Tumor invasion of the sympathetic plexus is uncommon. The majority of the cases, thus far reported, involve the hypogastric plexus, usually following cancer of the uterus. A rather thorough search of the literature fails to reveal a hitherto reported case of cancerous involvement of the solar plexus.

To explain the peculiar distribution of the cancerous invasion in this case, a study of the anatomical distribution of the lymph spaces of the nerves, as elucidated by Axel Key, and Retzius, Ranvier and Waldeyer, offers illuminating information. These authors showed that the lymph spaces of nerves are in direct communication with the subarachnoidal and subdural spaces and can be injected from these situations. They found that the lymph spaces of the nerves are arranged concentrically in the perineurium, from which they pass directly into the endoneurium and from here around each nerve fibre, so that each fibre is bathed, as it were, in lymph fluid. In no instances could

any communication be discovered between these lymph spaces and the lymphatics of the nerve trunk, which run in the epineurium.

With these facts in mind, we note how closely the cancerous infiltration in the case just reported simulates the distribution of the lymph spaces. This case may therefore be regarded as a pathological demonstration of the anatomical distribution of the lymph spaces of nerves.

The perineurium may therefore be regarded as a protection against invasion from the lymphatics externally to it. This explains the comparative immunity of involvement of the nerve bundles in carcinoma of the peripheral trunks of nerves and in infectious lymphangitis. It also explains the selective distribution of the toxins to the nervous system in tetanus.

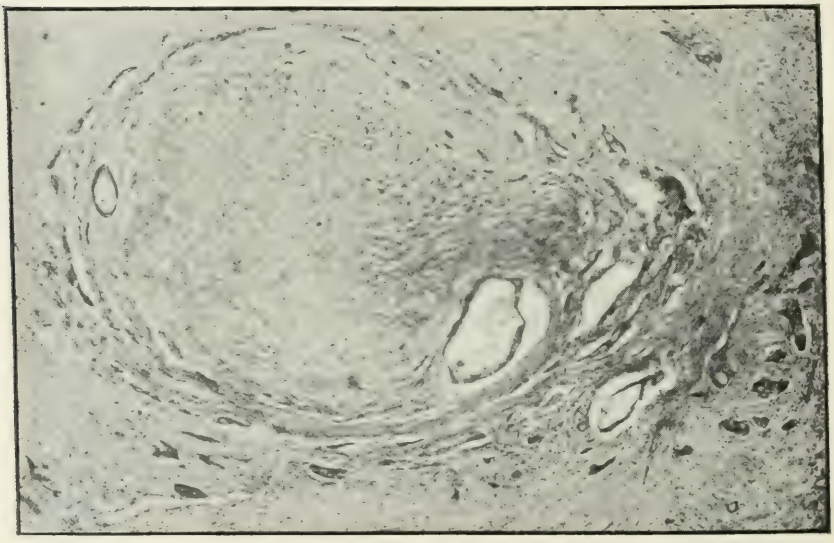


Fig. 1.—Showing Perineural Invasion by Carcinoma.

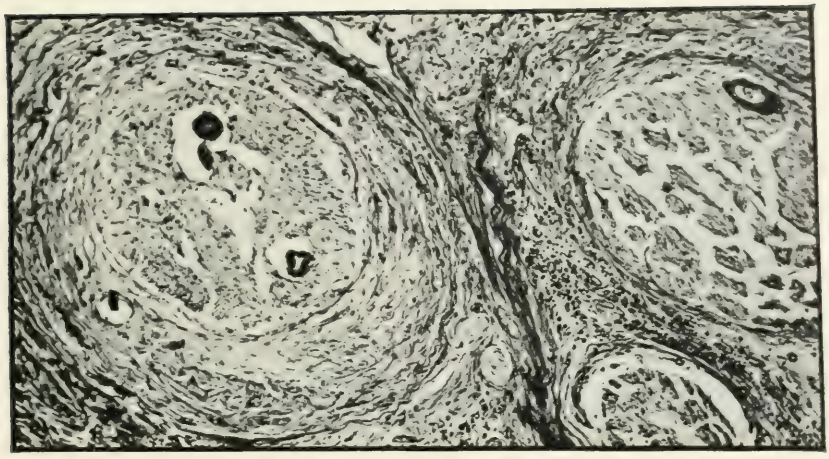


Fig. 2.—Showing Endoneural Invasion by Carcinoma.

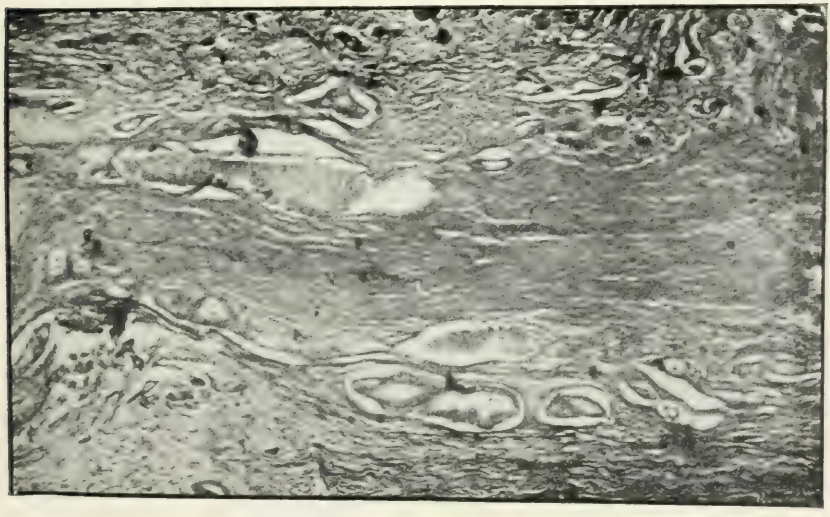


Fig. 3.—Showing Perineural and Endoneural Invasion by Carcinoma.

PRIMARY THROMBOSIS OF SUPERIOR MESENTERIC VEIN.

JAMES EWING, M.D.

Patient, male, 55 years of age, of temperate habits, without history or external signs of lues, and while apparently in excellent health, was suddenly seized with sharp pain in the lower lumbar region. The pain grew more severe and he was soon prostrated. Twelve hours later there was moderate general abdominal tenderness but no localized tumor. The bowels moved once moderately and the feces were decidedly acholic but apparently free from blood. No fever. Leucocytes 25,000, 80 per cent. polynuclear. This condition continued for 48 hours without definite change, but the pulse was notably weak from the first. On the third day there was a sudden turn for the worse with vomiting, collapse, and signs of peritonitis, and the patient died 72 hours after the first symptom. For this abstract of the history I am indebted to Dr. C. L. Gibson.

Necropsy.

Body of well-nourished male. Line of pubic hair ceases at pubes. General pilosity slightly below average. There are no other signs of Status Lymphaticus. No external markings. Slight jaundice. No oedema. Rigor moderate. Subcutaneous fat well developed. Abdomen slightly protuberant.

Blood cultures taken from right median basilio vein proved sterile on blood agar and plain agar, aerobic.

The peritoneal cavity contains about a pint of blood-stained fluid. A portion of small intestine measuring 177 c.m. in length occupying the intermediate portion of the lower ileum is black and infiltrated with blood. The peritoneal surface over this area is granular. The tissue is firm from distension of vessels. Its position is normal and none of the coils is confined by adhesions of any kind. It occupies the mid-abdominal region and presents beneath the omentum which is freely movable over the infarcted coils.

The entire mesentery leading from these coils is thickened and firm and the course of many vessels may be palpated as firm thrombosed cords. In the region of the pancreas there is a tumor-like mass in the root of the mesentery which on removal and incision proves to be the main mesenteric vein and branches, which are thickened, dilated and filled with a firm lamellated thrombus. The thrombus terminates above in a firm elongated free extremity at the level of the upper border of the pancreas. At this point also the wall of the vein is covered by a thin firmly adherent parietal thrombus (Adhesive Thrombophlebitis). Below, the thrombus is continuous with the black blood masses in the mesenteric border. The mesenteric artery is empty and contracted. The intestinal contents consist chiefly of dark, bloody fluid. The intestinal mucosa is dark, necrotic. On lifting the infarcted intestine out of the abdomen, it breaks apart near the center of the infarcted area.

An old thin fibrous band binds the coecum to the right side of the false pelvis. The appendix is normal.

Pancreas: Firm, hard, light colored.

Liver: Surface slightly irregular, mottled light areas with lines of deep congestion. Gall bladder contains a little bile. No calculi.

Stomach appears normal externally.

Kidneys: Size and consistence normal. Capsule strips, surface slightly granular. Markings somewhat irregular.

Adrenals: Normal.

Spleen: Large, soft, and very dark.

Remaining organs not examined.

Anatomical Diagnosis.

Primary thrombosis of mesenteric vein.

Infarction and necrosis of ileum. Beginning peritonitis.

Cirrhosis of liver.

Microscopical Examination.

The mesenteric vein from above the pancreas down to its bifurcation is the seat of an advanced productive inflammation.

All the coats of the vessels are involved, especially the media and intima. The adventitia is infiltrated with round cells, and new fibrous tissue, new vessels and round cells extend well out into the surrounding fat tissue. The media is much thickened with many collections of round cells, many new capillaries and much new fibrous tissue, new vessels and round cells extend well out into the surrounding fat tissue. The muscle bundles are atrophic and widely separated by oedema and hyaline connective tissue fibrils. The intima shows large areas of fibrous thickening. The lumen is occupied by a firm adherent mixed thrombus, in places containing many polynuclear leucocytes. The thrombus is adherent at many points along the main venous trunk. At several points there is beginning organization going out from the eroded intima. Where the vein comes in contact with the pancreas there is a saccular dilatation, the wall of which is very thin. The adjoining area of the pancreas is the seat of advanced interstitial productive pancreatitis.

The peripheral branches of the mesenteric vein down to the intestinal border are distended with blood in which there is little fibrin, while the vessel walls are not altered. Portions of the thrombosed mesenteric vein were stained by Levaditi's method for spirochaeta pallida, and although a prolonged search was made no spirochaetae were found.

The splenic vein is varicose, but the thrombus ends sharply at its junction with the mesenteric vein.

The mesenteric artery shows marked mesarteritis, with fibrosis, atrophy of muscle fibres, and many small mucous or fatty cysts.

The infarcted intestine is completely necrotic. Elsewhere the vessels are distended with blood. No old lesions were discovered in the intestines.

Pancreas shows moderate fat invasion. In many lobules there are areas of dense old fibrous tissue. There is no fat necrosis and the ducts are pervious. The pancreatic parenchyma is normal.

Liver shows distension of portal veins and occasional areas of fatty infiltration. The portal canals are often much thickened and infiltrated with round cells, especially about the portal veins.

Kidneys: There is well marked arteritis of the interlobular arteries; a few glomeruli are atrophied, but most of them are normal. The tubule cells are slightly degenerated.

Microscopical Diagnosis.

Mesenteric Thrombo-phlebitis.
Hemorrhagic infarction and necrosis of Ileum.
Chronic interstitial pancreatitis.
Arteritis of renal vessels.
Cirrhosis of liver.

Summary.

The study of the lesions in this case shows with entire certainty the course of events that led to the patient's death. A long established inflammation of a considerable portion of the mesenteric vein led eventually to a parietal thrombosis of this vein, beginning near the pancreas. This partial occlusion of the vessel led to venous stasis in the intestine, with pain and prostration. The parietal thrombus soon became complete during the 48 hours of the illness, and this was followed by complete strangulation and necrosis, which proved rapidly fatal.

The thrombosis is fully explained by the changes in the wall of the upper few inches of the vein, and there is no need to look for primary lesions in the intestine, which were found to be missing. The main thrombus was old (3 days), firmly adherent, and lamellated, the peripheral veins being gorged with blood without coagulation.

The cause of the phlebitis is not clearly indicated in the histological appearance of the lesion. The blood being sterile, there was no indication of general septicemia with local vascular lesions.

The commonest cause of localized chronic phlebitis is syphilis, and the lesions were somewhat similar to those which occur

in syphilis. As possible additional signs of syphilis there were old periportal cirrhosis of the liver, interstitial pancreatitis, and renal arteritis. Yet none of these lesions is pathognomonic of syphilis, and together they are inadequate to establish the diagnosis of syphilis. After syphilis, general arteriosclerosis suggests itself as the true explanation of the conditions disclosed. From this point of view one may attribute all the lesions found in the body to deterioration in the structure of the vessel walls with secondary changes in the organs. The changes in the liver and kidney seem most reasonably explained in this way rather than by syphilis. These lesions lack the pronounced character that one expects in syphilis, and seem to be chiefly degenerative with subsequent new growth of tissue. For the advanced stage of the lesion at the mesenteric region a special factor is needed, for which one might suggest a special congenital weakness of the vessels at this point. The splenic vein was unusually thin and tortuous. Or some special factor might be found in the patient's alimentary history. Therefore I would offer as the most probable explanation of the case: Arteriosclerosis of complex origin, not syphilitic, acting with special intensity on congenitally weak mesenteric vessels.

Study of the Literature.

The study of the literature serves to place the present case in its proper series among the forms of mesenteric thrombosis, and throws some light on the etiology.

Lissauer (*Virchow's Archiv.*, 1908, Bd. 192, p. 278) made an exhaustive study of 68 cases examined at autopsy in Breslau. He was able to find adequate causes of this condition in 92 per cent. of the cases as follows:

	Per Cent.
Cirrhosis of the liver	9
Syphilis of liver and mesenteric vessels	10
Cancer of liver	6
Cancer of stomach	10
Cancer of gall bladder	9

Gall stones (suppuration)	13
Diseases of pancreas	15
Diseases of spleen	7.5
Appendicitis	9
Intestinal cancer	3
Suppuration of navel	1.5
	92

In all but nine of the cases the etiology was clear, but in these nine there was no gross alteration in the vessel wall. In six of these nine cases the thrombosis was attributed to cirrhosis of the liver, and in three no definite etiology was established. In none of the nine doubtful cases was there a microscopical examination of the vessel wall. From this study it does not appear that primary thrombosis of the mesenteric vessels can occur without local lesions in the vessels, nor do I find that the old idea of a spontaneous thrombosis in the mesenteric vessels has any definite support in recent literature.

Our case certainly belongs in the group caused by primary phlebitis. Borrmann (*Deutsch. Arch. kl. Med.*, 1897, Bd. 59) discusses this group at length, reporting seven cases, in all of which he considers a luetic origin practically certain on account of the structure of the lesions and the presence of well marked sclerosis of the liver. The present case showed a phlebitis resembling a syphilitic lesion and peculiar cirrhosis of the liver, which might be syphilitic, and Borrmann would, therefore, probably have called it luetic.

As other possible causes of local productive phlebitis, Borrmann mentions old age, high arterial pressure, and alcoholism.

Our patient was not old, had no signs of Bright's disease, and was not alcoholic.

From this point one is reduced to references to clinical reports of diseases preceding primary mesenteric thrombosis and to other general causes of chronic productive phlebitis. Sprengel (*Arch. fur kl. Chir.*, Bd. 67, p. 587) analizes several cases from this point of view. In one there were varicose veins in

the legs. Our patient had a varicose splenic vein but no others, and this was probably connected with the mesenteric phlebitis. In three other cases, typhoid fever, severe diarrhoea, and pneumonia preceded the thrombosis by a few weeks or months, but our patient had none of these diseases.

Jackson, Porter and Quinby analize over 200 cases (*Jour. Amer. Med. Assoc.*, 1904, Vols. 42, 43). They find many cases of primary productive phlebitis, some of which were clearly syphilitic, but they do not discuss other sources of such phlebitis.

Deckart (*Mittheil a. d. Grenzgeb. d. Chir.*, Bd. 5, 511) analizes 67 cases of mesenteric arterial or venous thrombosis, and cannot decide why, in some cases, there is anemic infarction and in others hemorrhagic infarction of the intestine. The result does not apparently depend on which vessel is involved.

The frequency of primary mesenteric thrombosis high up in the superior mesenteric vessels suggests that this may be a weak point in the anatomical structure of the vascular system in certain subjects. At this point the large splenic vein receiving pancreatic and gastric branches unites with the superior mesenteric to form the portal vein. Here is a remarkable juncture of large veins draining the organs of digestion, and more or less influenced by changes in the position and function of these organs. It would seem reasonable to suppose that primary inflammation of the vessels at this point might occasionally result from traumatism, over-distension, irritation by digestive products, or from premature senile changes. A luetic origin need not be assumed for every case of primary productive arteritis or phlebitis, especially in this region.

In the present case, as in some of Borrmann's, all of the organic lesions might be referred to slowly advancing senile changes in the organs and vessels.

Borrmann and others fully recognize the necessity of recognizing arteriosclerosis with its complex etiology, as a prominent cause of mesenteric phlebitis and thrombosis. The present case seems to fall in this category.

A LARGE TUMOR OF THE LIVER, ASSOCIATED WITH A TUMOR OF THE OESOPHAGUS.

CHARLES NORRIS, M.D.

The liver and oesophagus which I show you came from a man 73 years old, with very little clinical history, except that he had been, up to middle age, a severe drinker, and three months before death he had epigastric pain and lost weight and became very weak.

At autopsy there was found a very large liver which practically occupied the right half of the upper quadrants of the abdomen. A clinical diagnosis of primary carcinoma of the liver had been made and, before I came across the tumor of the oesophagus, it seemed to me that that was a likely diagnosis, the tumor resembling some of the cases of primary carcinoma of the liver that I have seen. An interesting observation in this case is that, although the metastatic growth in the liver was so extensive, there were no metastases elsewhere with the exception possibly of one, say only 3 or 4 mm. in length by one mm. in breadth, on the pleura of the left lower lobe of the lung. No metastatic nodules were found in the other organs on microscopic examination.

The tumor in the oesophagus is situated at the bifurcation of the trachea, measuring 7 cm. in length by 3 cm. in breadth. About 1 cm. of the wall of the oesophagus is free from growth. There is no stenosis of the oesophagus. The portion of the trachea beneath the tumor of the oesophagus is uninvolved, the mucous membrane being normal in the gross.

The growth in the liver and oesophagus were identical as to their histology. I am unable to make up my mind, for the present, whether to call the tumor an epithelioma or a sarcoma.

Discussion.

DR. JAMES EWING: I had an opportunity to study these specimens in the gross and microscopically, and I came to the conclusions (of which I am not entirely certain) that Dr. Nor-

ris' interpretation is correct and that he is not dealing with primary carcinoma of the liver.

A more difficult point to decide is the true nature of the tumor. But, all things considered, it seems to me the chances are very much in favor of its being an embryonal epithelioma—it does not seem to me probable that a tumor in the liver of this sort could have reached the oesophagus in the region where we find this ulceration. The ordinary epithelioma of the oesophagus, however, show a tendency to extend toward the stomach and liver.

As Benecke has shown recently, some of the supposed implanted metastases of carcinomata in the stomach are to be explained as a result of extension through the lymphatics to the submucosa of the stomach, where they sooner or later protrude in the form of a flat tumor or ulcer.

The remarkable cell characteristics of this tumor are extremely interesting, but I think they suggest that the tumor has arisen from some embryonal group of cells in the oesophagus.

I ought to apologize for offering this somewhat positive opinion in the presence of Dr. Norris, who has studied the case more thoroughly than I have, but I know he was of this opinion up to recently and I think he can safely retain his original diagnosis.

SPECIMENS FROM A CASE OF BISMUTH POISONING.

GEORGE BAEHR, M.D.

Before showing the specimens from a case dying of bismuth poisoning, it is only necessary to mention a few points concerning the clinical course. The patient was a man 19 years of age, who one year before admission to the hospital had sustained some injury to his left hip. Following this he developed three suppurating sinuses, two of which were superficial and one deep. After entering the hospital he was operated upon, the

two superficial sinuses excised and the wound closed with sutures. The following week an attempt was made to dissect out the third sinus, but it was found to be too extensive. It was, therefore, decided to use Beck's paste injections as treatment. Three ounces of a 24½ per cent. suspension of bismuth subnitrate in vaseline were injected into the sinus. Five days after injection, the patient complained of salivation and sore gums. On the seventh day his gums showed a line resembling very closely a "lead" line, and two days later the patient developed a small ulcer under the tongue, which gradually spread along the course of the ranine vessels. Two weeks after the injection, he developed a large ulcer on both tonsils, which spread rapidly to the faucial pillars, soft palate, uvula and pharynx. It was of a dark grayish-brown color. The patient's breath at this time had a very foul odor, but not like that of tellurium, at one time a not infrequent impurity in bismuth salts. Three weeks after admission the blood picture was normal, except that it showed a secondary anemia and a marked stippling of the red cells, an observation which has not been described in any previously reported case of bismuth poisoning. Three weeks after the injection of the bismuth the patient developed a diarrhoea which became very marked, progressive anemia and emaciation, and died three weeks after the injection.

At autopsy, in addition to relatively insignificant parenchymatous changes in the various viscera, there was found an intense parenchymatous degeneration in the kidneys, which has been described in other cases and which is only equalled in cases of bichloride poisoning. The intestines showed a remarkable lesion. The mucosa from the ileo-caecal valve to the anus and including the terminal four inches of the ileum was completely necrotic, markedly thickened, and of a grayish-black color.

With microchemical tests particles of bismuth were not detected in any viscus. On gross analysis, however, the liver, spleen, kidneys and large intestine showed the presence of large quantities of bismuth and of no other heavy metal except iron.

The microscopic examination of tissues removed from side of the wound showed a very interesting condition. Large quantities of bismuth particles could be demonstrated by microchemical means in phagocytes in the wall of the sinus. These phagocytes filled with small particles of bismuth were to be seen invading the deeper tissues and even the muscle, suggesting a mode of entry of the bismuth into the body.

Discussion.

Dr. Larkin: Because of the close resemblance of the lesions described to those caused by bichloride of mercury, Dr. Larkin wished to know whether the chemical examination had included a search for mercury or arsenic. He rather questioned the probability of an innocuous substance, such as bismuth subnitrate, causing such extensive lesions.

Dr. Frank: There are quite a number of cases on record where after the injection of Beck's paste, bismuth poisoning has developed. There is no question but that quite incontestable cases have occurred.

Dr. Baehr: Not only was the Beck's paste carefully analyzed for other metals (lead, arsenic, antimony, zinc and mercury), but the urine, stools and all the viscera were similarly analyzed and nothing else found besides the bismuth which could possibly produce the picture. The urine and stools throughout the clinical course also contained large quantities of bismuth. Beck advises washing out the sinus with olive oil; but in this case it proved of no avail. It has been suggested that the intestinal lesion resembles that of bichloride poisoning. This must be admitted. But the line on the gums in this case resembled the "lead" line, but that does not make the condition lead poisoning.

It surprises me that the pathogenesis of this condition should be questioned. Merck's chemically pure bismuth, which upon subsequent analysis was proven to be chemically pure, was injected into the sinus. Considerable quantities of bismuth but

of no other heavy metal were recovered from the liver, spleen, kidneys and large intestine post-mortem.

Concerning the remarks of one of the gentlemen, relative to the conception of bismuth subnitrate as an innocuous substance, I desire to report that during the past few months at Mount Sinai Hospital we have had the opportunity of observing two other cases of bismuth poisoning which recovered. Complete details of these two cases and of the case under discussion this evening will be published shortly by Dr. Mayer and myself.

Poisoning by bismuth is not rare. The literature contains reports of almost seventy undoubted cases. When administered by mouth the poisonings have chiefly occurred in young children in whom, because of decomposition of the subnitrate by bacteria, the symptoms have been those of nitrate poisoning. The majority of instances of bismuth poisoning have followed injections into sinus cavities, and nearly all of these have been entirely due to the bismuth radical.

Experimentally, extensive work has been done to prove definitely the toxicity of bismuth. The most important has been done by Meyer and Steinfeld and by Schmelzer. The latter did his work in Kobert's laboratory and Kobert, in his book, has accepted this work as conclusive. The lesions in the intestines, obtained by Meyer and Steinfeld, in some of their experiments, correspond in most details with those shown this evening. In fact, of the cases of bismuth poisoning coming to autopsy that have been reported, this one corresponds most accurately to the results obtained in most of the experimental work.

DEMONSTRATION OF THE CARDIAC LESIONS OF SUBACUTE BACTERIAL ENDOCARDITIS.

E. LIBMAN, M.D.

My object in showing you this collection of hearts to-night is fourfold. The main reason is that I believe that Dr. Baehr's demonstration of the glomerular lesions of subacute bacterial endocarditis will be made clearer if you at the same time see the cardiac lesions. The second object is that I want to demonstrate that the lesions in the cases in which the mitral valve is involved are quite characteristic of the infection by the attenuated coccus found in most of these cases. Thirdly, I hope to convince you that there are three stages of the disease in a number of the cases—the bacterial, abacterial healing, and abacterial healed stage. In the fourth place, I would like to point out to you that at least some of the cases which we have been wont to call "chronic endocarditis with fever" are examples of the healed form of the disease. For healing from a pathological standpoint does not necessarily remain recovery from a clinical standpoint.

The term "subacute bacterial endocarditis" I have adopted instead of the older terms: "chronic ulcerative endocarditis," "chronic malignant endocarditis," "chronic infectious endocarditis," etc. I call all cases of endocarditis which are proven due to bacteria (rheumatism is not so proven) "bacterial endocarditis" and divide the cases into "acute," "subacute," or "chronic," according to their clinical course. Many of the cases that belong in the group of which we are speaking to-night last only four to six months and are, therefore, certainly subacute and not chronic. Some may prefer to apply the term "chronic" to cases that last over one year.

We have had the unusual advantage of seeing a very large number of cases of the disease under discussion, and in 64 cases in which cultures were made during life, 94 per cent showed the attenuated cocci* ("streptococcus viridans" of Schottmueller).

*See discussion of Dr. Larkin's presentation, at the November meeting, by E. Libman.

In three cases the influenza bacillus was found, and in one the gonococcus. Once the cocci were found in the vegetations post-mortem, the cultures taken during life being all negative. Twice the cocci were found in the vegetations only, no cultures having been taken intra vitam. The gonococcus case does not properly belong in the group, as the case was of a rather acute type. It is included, however, for comparison, because the lesions in the heart were much like those characteristic of infections by the attenuated cocci.

In seven cases which we believe belong in the groups of subacute bacterial endocarditis, but which are in a healing or healed stage, the lesions were found bacteria-free. And of those cases among the seven in which cultures were made during life, they were negative.

(Dr. Libman now demonstrated the lesions in forty-one hearts belonging to the group.)

As you have seen, when the mitral valve is involved in these cases (and it is involved in the larger number of the cases), there is a tendency for the vegetations to spread upon the left posterior wall of the auricle, rather than on the valve edge. Very often the chordæ tendineæ attached to the posterior flap are covered to a greater or lesser extent by vegetations. Nearly always the anterior flap is also involved, and here the vegetations tend to grow down over the chordæ tendineæ, the involvement of the latter being often very extensive. Not uncommonly the chordæ tear, the torn ends being massed together by vegetations at the edge of the flap or the lower ends lying loose near the papillary muscles. The vegetations are yellowish, greenish, pinkish, or reddish in color, and vary much in size in different cases. As they grow older they become firmer and assume a more grayish color.

When the aortic valves are involved, the lesions are usually not characteristic and their extent is very variable. There may be only a small vegetative mass on one or more flaps. On the other hand, there may be enormous green masses that must block the orifice to a certain extent. The vegetations have a tendency

to extend down over the endocardium at the position of the septum membranaceum, and over the ventricular aspect of the aortic flap of the mitral valve and down over the chordæ tendineæ. There may develop an aneurism of the aortic flap of the mitral valve. Ulceration of the aortic valves at times occurs.

The frequency of involvement of the valves, the left auricle, and the chordæ is as follows:

	Cases.
Auricle, mitral valve, and chordæ	17
Auricle, mitral valve, chordæ, and aortic	5
Auricle and mitral valve	2
Mitral valve and chordæ	1
Aortic valve only	3
Aortic valve, chordæ, and oartic flap of mitral	4
Mitral, chordæ, and aortic	1
Auricle, mitral, and aortic	1
Total	34

The auricle was involved 25 times, the mitral valve 27 times, the chordæ 28 times, and the aortic valve 9 times. The frequency of the involvement of the chordæ and auricle is very striking. The lesions which we consider so characteristic in the group of cases, we have not found in a large series of cases of endocarditis due to the streptococcus, the pneumococcus and the staphylococcus. And, as in the present group of cases, most all are due to the attenuated cocci; the lesions must be considered characteristic of infection by these cocci. Other observers have noted similar lesions in small groups of cases I will discuss their observations in a later paper.

After I had made these observations, I found lesions in the case (which I now demonstrate to you) of a man who died with the clinical picture of uremia, which I considered to be the healed form of the lesions I had previously found in cases of infection by the attenuated cocci. There were, as you see, extensive healed lesions of the auricular wall, and the chordæ tendineæ attached to the anterior flap are torn, and are thickened,

fibrous and in part calcareous. My opinion that these were healed lesions of subacute bacterial endocarditis (in all probability due to the cocci, as they cause most all of the cases) was confirmed recently by Dr. Baehr's studies of the kidneys, in which he found the pathognomonic glomerular lesions (in a healed state). Later I came across two further cases. On going through my collection carefully I found that partial healing occurs in many cases, and that partial healing can occur even while there are still bacteria in the blood.

Last summer I had a case in the ward that belonged clinically in the group usually called "cases of chronic endocarditis with fever." The clinical phenomena led me to suspect that the case was one of healed subacute bacterial endocarditis and that the continuance of the clinical phenomena was due to the fact that there was a large calcareous mass on the aortic valve from which pieces were continually breaking off, the calcareous mass representing the healing of a large mass of vegetation. At autopsy the conditions of the aortic valve was as suspected during life, and Dr. Baehr found pathognomonic healed glomerular lesions. I show you now specimens from two other cases of a similar nature which were in our collection, and which we now have proven by study of material from the kidneys, that they are instances of healed subacute bacterial endocarditis. One can not diagnose that a case is abacterial simply because the blood cultures are negative, for I have seen one case in which five blood cultures were negative and still the heart post-mortem shows a lesion which was at least in part active.

I now have under observation several clinical cases that I believe represent the healed form (from a pathological and bacteriological point of view) of the disease under question. I shall later report on the clinical picture and the diagnostic points. I may say now that some pass as cases of chronic nephritis complicating chronic endocarditis.

There is very little in the literature concerning the healing of this disease. Latham describes a case which recovered after a number of cultures had been positive. Reiche describes one

such case which died of an aneurism of an intrahepatic branch of the hepatic artery, having had negative cultures after a number were positive. He states that the cardiac lesions were healed, but does not describe them. Osler, Horder, Rosenow and Schottmueller do not seem to have met with healing or healed cases. Lenhartz described two cases, but they were not followed up. After I had announced this demonstration, my attention was drawn to a paper by Harbitz.* He, in the extensive pathological study of endocarditis, found ten instances of what he thought represented healing forms of bacterial endocarditis.

Apparently many cases recover spontaneously. They must be short in duration, and have but few symptoms and are therefore not suspected of having any infection. Perhaps many such patients do not feel sick enough to call in a physician. The cases which we see with positive cultures do not usually recover. We do see cases become abacterial, but they usually die in a short time from embolisms, anemia, exhaustion, decompensation, or other causes. I had one patient with influenzal endocarditis, in whom three cultures were negative after five were positive. He died later of anemia and decompensation.

Discussion.

DR. LARKIN: I should like to ask Dr. Libman if all the cases of malignant endocarditis which he described to-night are those which have been implanted on chronic cardiac valvular lesions, or if he has seen any of the lesions in which the endocarditis coccus was implanted on previously normal valves?

DR. PAPPENHEIMER: I should like to ask Dr. Libman whether he believes that the lesion begins on the auricular wall and extends down to the valve? He mentions several specimens that show healing, in which the reparative process is most advanced on the auricular wall.

DR. MOSCHOWITZ: I should like to ask Dr. Libman whether he has been able to trace the source of infection?

*Deutsche med. Wochenschr., 1899.

Dr. Libman—Answer to Dr. Larkin: Nearly all of these infections occurred in valves that were previously diseased.

Answer to Dr. Pappenheimer: I am inclined to believe that the process begins near the free margin of the valve, and extends upwards on the auricular wall. In several instances the reparative process is most marked in the upper part of the lesion.

Answer to Dr. Moschowitz: We have not yet made extensive studies on the source of infection. We believe that the organisms may gain their entry through the throat; English authors seem to think that the intestines represent the site of entry. The important point is that we had not hitherto recovered the attenuated cocci in the blood except in cases of endocarditis. And in none of these cases do we find an inflammatory focus anywhere in the body which represents the portal of entry. It is therefore important that one be very careful before instituting any operative procedures in cases in which these organisms are found in the blood, because foci which might clinically impress one as being a possible source of invasion, are really the results of embolic processes.

GLOMERULAR LESIONS OF SUBACUTE BACTERIAL ENDOCARDITIS.

GEORGE BAEHR, M.D.

It seems remarkable that such a distinct pathological picture as is present in this disease of the glomeruli of the kidney should have been almost universally overlooked. Clinically, it has been known to many observers who have had a number of cases of this disease, that hematuria was almost a constant phenomenon, at least microscopically, but usually interpreted as indicating a hemorrhagic nephritis. Lenhartz, for example, in his original paper and in his book in describing four cases of

chronic bacterial endocarditis mentioned the occurrence, and Harbitz in 16 cases made a special point of the association of nephritis hemorrhagica with this disease. Similarly, Heubner, Romberg and Horder have made note of the almost constant occurrence of hematuria in this disease.

That the disease was not overlooked before Loehlein's original paper in which this lesion was described, is shown by the fact that Aschoff described a glomerular lesion which in some details resembled the one to be presently described, but which he included in the classification of acute glomerulo-nephritis. In speaking of the etiology of acute glomerulo-nephritis he mentions ulcerative endocarditis as one of the commonest cases. According to our experience, lesions of the glomeruli are ordinarily not present in the acute ulcerative endocarditis, and his cases were therefore probably chronic. Aschoff does not, however, associate the glomerular lesion with his cases of chronic "ulcerative" endocarditis.

In Loehlein's original paper on inflammatory diseases of the glomeruli, the same type of glomerular lesions which forms the subject of this presentation was described, but was classified by him in his group of subacute glomerular nephritis, although he noted some essential differences and noted that in both instances the individuals in whom the lesions were found suffered from chronic ulcerative endocarditis. At that time he thought the lesion due to some toxin of the disease. He redescribed these cases in 1910 and added six others, considering them as a distinctive type of hemorrhagic nephritis and expressing the opinion that the lesions were embolic in nature. In none of his cases, however, was he able to demonstrate bacteria in the affected glomeruli. The reason that he took this view as to the embolic nature of the process was because in one of the larger arteries in one of his sections, there was an embolus which completely occluded the lumen and which contained large numbers of streptocci.

The reason that the lesion has been overlooked is probably because few people had the opportunity of studying a large series

of cases. This work has only been possible because of the extensive collection Dr. Libman has made during the past few years.

To be clear upon the etiology of this lesion, it is necessary to understand one or two points concerning the cultural characteristics of the coccus which is one of the commonest causes of this disease. On slant serum-agar it forms a very dry growth, and in broth it grows in very dry clumps which are difficult to break, even by shaking. On the vegetations it similarly grows in small clumps in immense numbers; it is therefore quite possible that the constant stream of blood washing over these vegetations will wash off some of these clumps. This organism has been called by Schottmueller the streptococcus viridans, though more recently Rosenow has produced some evidence which suggested that it is a modified pneumococcus rather than an attenuated streptococcus. Libman and Celler, on the other hand, have shown that this organism possesses characteristics of both the pneumococcus and streptococcus, so that the possibility now exists that it may belong in a group intermediate between the two organisms. Until its status is settled, it would be best to adopt Libman's suggestion and speak of the organism in question as the endocarditis coccus of subacute bacterial endocarditis. There is just as much justification for this as there is for calling the diplococcus lanceolatus the pneumococcus.

With one exception the kidneys from the thirty-four cases of subacute bacterial endocardits included in this series were obtained from Dr. Libman's collection. Twenty-seven of these cases were in the bacterial stage, the endocarditis coccus being recovered from twenty-five cases (twenty-two by blood culture during life and three by cultural and miscoscopic examination of the vegetations). In one case the B. influenza was obtained in blood cultures, in another the gonococcus. For this last case I am indebted to Dr. Asch, of the German Hospital.

Glomerular Lesions: The salient features of the pathological picture are, firstly, the involvement of one or more loops of a variable number of glomeruli; secondly, the absence of any

visible disease in uninvolved glomeruli, and in the uninvolved portions of affected glomeruli; and thirdly, the association in most of the bacterial cases of all the various stages of the lesion in any one microscopical section.

The very earliest stage of the lesions consists in a swelling of the glomerular epithelium of one or more loops. The swollen cells very soon fuse into a solid mass consisting of a finely granular structureless material in which a few nuclei may still be visible. This granular mass may affect loops at the periphery or in the center of the glomerulus. With hematoxylin it usually takes a deep-blue stain which renders it conspicuous; with Van Gieson's stain it is colored a reddish-brown, or golden-brown, contrasting sharply with loops of other glomeruli which show a later stage. If the process affects loops at the periphery of the Malpighian tuft, the epithelium of the visceral layer of Bowman's capsule undergoes swelling, often some proliferation, and usually desquamation into the capsular space. When the mass with its overlying epithelium comes into contact with the parietal layer of Bowman's capsule, the latter then also may take a share in the proliferation and desquamation.

Eventually this proliferated and desquamated epithelium, which seldom is very extensive, undergoes necrosis as did the previously swollen epithelium of the involved loop of the glomerulus. Then the entire disintegrating mass fuses with the Bowman's capsule and often is seen to become somewhat separated from the remainder of the glomerulus and to become flattened out over the Bowman's capsule in crescentic fashion.

In many pictures like the latter, the finely granular cellular material is seen to be traversed by a very delicate pink staining network. The adjacent interstitial tissue by this time usually shows evidences of some proliferation and is often the site of a small collection of round cells. Fibroblasts may occasionally be observed which are invading the amorphous debris from the connective tissue, and are actively taking part in the production of this fibrillar network. In the same microscopical section, loops of other glomeruli can be seen which are in a still later

stage of the process. Here the fibrillar network has thickened to such an extent that it has entirely replaced the necrotic material (except for a few epithelial nuclei), the mass now consisting of dense fibrous tissue. With the single hematoxylin stain this appears as a characteristic wedge of hyaline tissue containing a few nuclei.

Simultaneous with the replacement of the cellular debris by this connective tissue network, there occurs an active growth of the epithelial cells of the adjacent intact portions of the parietal layer of Bowman's capsule. They advance over the inner aspect of the necrotic mass which by this time has usually separated somewhat from the rest of the glomerulus. The result eventually seen represents the healed stage of the lesion; a hyaline mass having roughly the shape of a truncated pyramid, its base fused with the adjacent interstitial tissue, its mesial aspect adherent to the remainder of the glomerulus, its sides clothed by a reflection of the adjacent epithelium of Bowman's capsule.

The portion of the glomerulus involved may be very much larger than here described; it may be a large segment or even the entire Malpighian tuft. In such a case the entire Malpighian body may become converted into a hyaline fibrous body in the peripheral portion, of which the fibrillar tissue may show a tendency toward a crescentic arrangement.

The proportionate number of glomeruli involved varied from 2 to 75 per cent. The average of all the cases studied was 26 per cent. In only two cases among the twenty-five due to the endocarditis coccus, were no glomerular lesions discoverable, although in one case seven and in the other nine blocks taken from various parts of the kidney were examined. Both cases, as far as could be determined, were of very brief duration, though whether this or other factors were the reason for the absence of the lesions, could not be ascertained. In one case due to the B. influenza and one due to the gonococcus, no glomerular lesions were found.

Two other cases among the twenty-five due to the endocarditis coccus, showed a severe disease of the glomeruli, but the

pathological picture resembled that of a glomerulo-nephritis. There are reasons, however, for considering the possiblity that the lesions in these cases were also of embolic nature. For the present if we exclude these two cases and the two in which no glomerular lesions were found, twenty-one of the twenty-five cases of subacute bacterial endocarditis due to the endocarditis coccus showed the typical pathological picture in microscopical sections of the kidneys.

In these sections all stages of the glomerular process was usually visible. The early lesions were exclusively present in two cases, the healed in one. In some of the remainder the early stages predominated, in others the late or healed stage.

In the collection which he has exhibited this evening, Dr. Libman has seven hearts which he has for some time considered as typical of the abacterial healing or healed stage of subacute bacterial endocarditis. His opinion was based upon the clinical course of the disease in these individuals, the character of the vegetations and their site. This view received substantial confirmation by the finding of the healed stage of the glomerular lesions in the kidney in six of the seven cases. In the seventh case the glomeruli showed a very marked hypertrophy and a hyaline thickening of the capillary walls in all the Malpighian tufts. Microscopically the kidney presented the typical picture of a secondary contracted kidney. The glomerular change closely resembled that described by Loehlein in secondary contracted kidneys as an antecedent of acute glomerulo-nephritis.

Conclusions.

1. In most cases of subacute bacterial endocarditis, due to the endocarditis coccus, a typical pathological picture is present.

2. In two examples of this disease caused by other organisms, the glomeruli appeared normal.

3. In a group of cases having vegetations which are typical of those in the active stage of subacute bacterial endocarditis, except that they are abacterial and healed, the healed stage of this distinctive glomerular lesion is present.

4. These cases therefore are most probably examples of subacute bacterial endocarditis due originally to the endocarditis coccus, but in which the endocardial vegetations have become abacterial and are healing or healed.

The complete results of the preceding study will later be published in the *Journal of Experimental Medicine*. Details of the work have been omitted as much as possible in this evening's presentation and the conclusions presented as briefly as possible.

For the lantern demonstration, I have to thank Dr. Mandelbaum, who very kindly made the execllent negatives from which the lantern slides were copied. I am indebted to Dr. Libman both for the pathological material with which the study was made and for much helpful advice during its course.

Discussion.

DR. LIBMAN: Dr. Baehr has inadvertently omitted one of the most important matters in the whole discussion, and that is his extensive studies on the kidney lesions in acute bacterial endocarditis. As he wil tell you, in acute bacterial endocarditis he has never found glomerular lesions such as are found in cases of infection by the attenuated cocci. This means that this kidney lesion is practically pathognomonic of the infection by the endocarditis cocci.

As stated above, the gonococcus case was really not a subacute case. It was only included because the lesions in the heart were similar, and I therefore thought it would be of interest to see whether Dr. Baehr would find lesions in the kidneys similar to those found in subacute bacterial endocarditis.

Dr. Baehr and I will later report on the question of whether the number of lesions in the glomeruli have any relationship to the number of bacteria in the blood. As you have heard, there were two cases with positive bacteriological findings post-mortem, in which no glomerular lesions were found. In one of these cases there were hardly any bacteria in the blood, and in the other case, although five blood cultures were made, they were all negative.

As regards the symptoms which are due to the renal lesions in these cases, they are of great interest clinically. Some of the patients have erythrocytes in the urine; some have marked hematuria; some present the clinical picture of nephritis. Sometimes renal and vesical symptoms are so marked that cases have been diagnosed as being instances of tuberculosis of the kidney or of calculus disease or of pyelitis, and I know of one instance in which the kidney in such a case was removed because it was supposed that the patient was suffering from severe pyelonephritis.

Dr. Baehr: My omission to mention the examination of the kidney glomeruli in the cases of acute-bacterial endocarditis was unintentional. Fifty-four cases of acute endocarditis were studied, the majority of which were of bacterial origin and in none was a single glomerulus found which could be identified as in any respect similar to the typical condition in this disease.

When in acute endocarditis bacterial emboli do occur in glomeruli, they produce a suppurative lesion there. The endocarditis coccus has absolutely no chemotactic action, and therefore the lesions in the kidneys are non-suppurative and they assume this typical appearance.

DEMONSTRATION OF OX-HEARTS SHOWING INJECTION OF THE CONDUCTION SYSTEM.

ALFRED E. COHN

(From the Hospital of the Rockefeller Institute for Medical Research.)

Several ox-hearts were shown. Black India ink was injected into the left division of the auriculo-ventricular bundle. Injection below the undefended space was occasionally successful. Usually the spaces through which the India ink passed were difficult to meet with in this location. It was found easy to insert the small needle into one of the spaces about the ramifications of the apex of the ventricle, where their situation is clearly

visible. When necessary, several such places were sought for, and the injection of the whole system completed. A demonstration of the nature of the arborization of the system is satisfactory only when the injection of the ink takes place before the left division has divided, at the site already mentioned. In the hearts shown both methods had been employed. India ink was used as the injection fluid because it, unlike a number of dyes which had been employed, did not spread into a diffuse stain.

The ink flows through channels which follow the course which Aschoff and Tawara have described as that of the A-V system. When the injected specimen is examined, the left branch appears as an undivided stem, under the endocardium of the left ventricle, a short distance below the aortic ring emerging just below the subaortic muscle. It divdes in two portions which pass toward the posterior and anterior papillary muscles and from them to the venous and arterial bases of the ventricle. The apex and the portion of the ventricle lying between the papillary muscles may be supplied by branches arising separately from the left division. It is quite clear in the light of these preparations that an impulse conveyed over this system must arrive first at the region of the papillary muscles and later at the base. This distribution of the system coincides with the conception that the papillary muscles of the heart contract before the other portions.

The spaces through which the injection fluid passes is not quite clear. The bursa-like spaces described by Curran may be the ones traversed. The distribution excludes the arterial, venous, or lymphatic systems from being channels employed. About the larger branches a single space only is injected. The method of injection proves the continuity of the whole system.

Discussion.

Dr. B. S. Oppenheimer: After hearing of the method through Dr. MacCallum, I injected a few hearts of ungulates with India ink diluted with water, but the injections were not so complete as Dr. Cohn's. A microscopic section of the ven-

tricular wall at a point distant from the site of injection, showed that the spaces around the Purkinje fibers only had been injected. The India ink had also penetrated between the individual Purkinje fibers to a certain extent, outlining them.

FALSE GIGANTISM, MAINLY AFFECTING THE BONES, COMPLICATED BY TRAUMATIC OSTOSES.

JOHN C. A. GERSTER, M.D.

This eleven-year-old boy has no positive facts in his history up to three months ago, when he fell from a wagon, striking his right leg. A swelling promptly appeared at the site of the injury and has persisted there ever since. Two months after the accident, the boy's parents brought him to the University and Bellevue Hospital Medical School's Clinic, asking why it was that the injured leg had grown larger, and why it was that the foot on that side required a shoe two sizes larger than the one of the other side. At the time of application to the clinic there was no pain, fever, loss of weight, or function. There was a limp, due to unequal length of the limbs.

Examination showed the right lower extremity longer than the left, the thighs, however, of equal length, but the right leg one and one-quarter inches longer than the left. The right foot was larger in all dimensions than the left. Two hard, smooth, oval, bony protuberances were felt, immovably attached to the middle third of the tibia. They were absolutely painless. Function of the leg was perfect. The rest of the physical examination revealed nothing of special interest.

X-ray findings: The right tibia and fibula are 1¼ inches longer than the left. There are two subperiosteal bony tumors of the tibia, one the size of a pigeon's egg, the other slightly smaller. The shaft is apparently healthy. The right fibula shows an irregular, diffuse, periosteal thickening as compared to

the opposite side. I should like to call attention to certain lines which appear in X-ray plates of long bones in children. These lines lie parallel to the epiphyseal lines and at irregular distances one from the other, but, if the bones of both sides are compared it will be seen that the position of the lines is symmetrical. It may be possible that these lines show periods when growth was arrested and a more intense local bony deposit occurred.

As just said, in normal individuals these lines are symmetrically placed; in this boy's tibiae *the lines on the affected side (although approximately symmetrical) are further apart than on the opposite side.* I take this to indicate that the affected bones have been steadily outstripping their opposite companions ever since very early life.

X-ray plates of the feet show that the entire skeleton of the right foot is larger than that of the left, and measurement of the right os calcis and astragelus show them larger in all dimensions than those of the opposite side. In short, the bony skeleton of the right lower limb, from the knee down, is distinctly larger than that of the left side.

X-ray of the skull shows no enlargement of the pituitary fossa.

Blood examination revealed a slight secondary anaemia. Three Wasserman and one Noguchi reactions were made, all with negative results.

A specimen for microscopical examination was removed; this consisted in a piece from the larger of the two bony masses on the tibia, with some of the adjacent soft tissue.

The report was as follows:

"Microscopical examination of the bone reveals some sclerosis of the cancellous spaces. Microscopical examination of the soft tissues removed from the immediate vicinity of the bone reveals a quantity of poorly nourished fibrous tissue in which are a number of empty vascular spaces apparently of lymphatic nature. There is nothing in the histology to indicate the presence of syphilis or of a new growth.

"SYMMERS, Pathologist."

These tumors seem to me to have been subperiosteal effusions of blood at the time of injury which subsequently became organized into bony tissue—traumatic ostoses.

In short, there is a hypertrophy of part of the bony skeleton (from the right knee down), complicated by the presence of two traumatic ostoses.